Identifying Types of Research Materials: Primary, Secondary & Tertiary

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Types of Research Information

• **Primary Sources**
  Primary research articles report new findings & conclusions

• **Secondary Sources**

• **Tertiary Sources**
Types of Research Information

Primary Sources

- **Original documents, such as:**
  - Scholarly articles reporting new findings
  - Diaries and autobiographies
  - Speeches
  - Letters, minutes, interviews
  - Video footage
  - Official records

- **Creative Works, such as:**
  - Poetry
  - Drama
  - Novels
  - Music
  - Art

- **Relics or artifacts, such as:**
  - Jewelry
  - Pottery
  - Furniture
  - Clothing
  - Buildings
Recognizing a Primary Research Article

Most research articles have the following sections:

• Abstract
• Introduction/Background
• Purpose of study
• Review of the Literature
• Methods
• Data Analysis
• Discussion of the Results
• Limits of the Study
• Suggestions for further research
• Conclusion
• References
BREAST CANCER AFTER PROPHYLACTIC BILATERAL MASTECTOMY IN WOMEN WITH A BRCA1 OR BRCA2 MUTATION

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THE identification of the breast-cancer-susceptibility genes BRCA1 and BRCA2 has sparked widespread interest in genetic testing and has led to an increased focus on genetic counseling and risk reduction strategies. Among women at risk for a mutation in these genes, we have found that 57 percent of women without breast cancer who had a 50 percent chance of carrying a BRCA1 or BRCA2 mutation requested genetic testing. This result indicates the need to determine the efficacy of the various options for reducing the risk of breast cancer and for early detection in women with a BRCA1 or BRCA2 mutation.

Women with a BRCA1 or BRCA2 mutation have a cumulative lifetime risk of ovarian cancer (up to the age of 70 years) of 55 to 85 percent and of invasive epithelial ovarian cancer of 15 to 65 percent. In these women the risk of breast cancer begins to increase near the age of 25 years, and their overall survival once breast cancer is diagnosed is similar to that of age-matched women with sporadic cases of breast cancer in both, the 10-year survival rate is about 50 percent.

Current risk-reduction strategies for women with a BRCA1 or BRCA2 mutation include regular surveillance; prophylactic mastectomy, oophorectomy, or both; and chemoprevention. In our experience, 50 percent of women who have a BRCA1 or BRCA2 mutation have chosen to undergo prophylactic bilateral mastectomy. Until now, however, there have been only retrospective studies of the efficacy of the procedure in women with an increased risk of breast cancer.
cancer on the basis of the family pedigree and not DNA testing.\textsuperscript{12}

We investigated the efficacy of prophylactic mastectomy in women with a proven pathogenic \textit{BRCA1} or \textit{BRCA2} mutation. Because a randomized trial is impossible for ethical reasons, we performed a prospective cohort study of women at a single institution who chose either prophylactic mastectomy or regular surveillance.

**METHODS**

**Study Subjects**

Beginning on January 1, 1992, we studied all women with a \textit{BRCA1} or \textit{BRCA2} mutation who were being monitored for breast cancer because of familial clustering of breast cancer, ovarian cancer, or both at the Danish Heritable Breast Cancer Center in Rønning, the Netherlands. We included all women who had been given a molecular diagnosis before January 1, 1998. Women with a \textit{BRCA1} or \textit{BRCA2} mutation in whom breast cancer developed before January 1, 1992, and one woman in whom breast cancer was diagnosed at first screening were excluded. The date January 1, 1992, was chosen because at that time, a multidisciplinary team at our family cancer clinic took over the care of women at high risk for breast cancer. A total of 189 women fulfilled the criteria. Eventually, 76 of these chose to undergo prophylactic bilateral mastectomy before the end of the follow-up period (March 1, 2003), whereas the other 65 women chose to continue regular surveillance. In all but two women prophylactic mastectomy was performed after the molecular diagnosis was established.

**Data Collection and Follow-up**

Information on vital status and the occurrence of cancer was extracted from the medical records of all women who were regularly monitored at our clinic until March 1, 2001, and were enrolled in a clinical research program approved by our medical ethics committee (protocol 98-37-17, updated in 1998). We obtained pathology reports of all mastectomy specimens and of all breast-biopsy specimens from the women who were being monitored. Information on prophylactic mastectomy performed for any reason (mainly at other clinics) was obtained from the women themselves and was verified by a review of all medical records. Truncating prophylactic mastectomy was defined as bilateral mastectomy before the age of 56 years and was performed prophylactically in the case of 55 women, for benign disease in the case of 1 woman, for ovarian cancer in the case of 7 women, and for cervical cancer in the case of 1 woman (Table 1). No women were lost to follow-up after prophylactic mastectomy. Of the women in the surveillance group, three died of ovarian cancer and two chose to be monitored at another hospital for practical reasons.

**Surgical Techniques and Surveillance**

In all cases, standard, bilateral, simple total mastectomy (including the nipple) was performed by a surgical oncologist at the Danish Heritable Breast Cancer Center. In 76 of the 76 women, the breasts were reconstructed with silicone prostheses by a plastic surgeon in the same session, followed later by a nipple reconstruction.

According to national guidelines, regular surveillance for breast cancer consists of a monthly breast self-examination, a clinical breast examination every six months, and yearly mammography. Since 1998, magnetic resonance imaging (MRI) has been an option at our clinic for women with mammographically very dense tissue and/or at high risk for breast cancer. In the current study, MRI was performed only for women with a history of previous invasive breast cancer.

**Analysis of \textit{BRCA1} and \textit{BRCA2} Mutations and Histologic Examination**

DNA analysis was performed according to standard procedures.\textsuperscript{13} \textit{BRCA1} and \textit{BRCA2} linkage analysis was used until 1994 and 1995, respectively, to identify the presence of hereditary breast cancer. From 1994 to 2003 we used direct mutation analysis. All \textit{BRCA1} and \textit{BRCA2} mutations were pathogenic, since they resulted in a premature truncation of the \textit{BRCA1} or \textit{BRCA2} protein.

Mastectomy specimens were examined histologically to rule out the presence of occult breast cancer. From each quadrant of the specimen, microscopical sections from these random blocks were examined according to standard procedures.

**Statistical Analysis**

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### Table 2. Characteristics of the Eight Women in the Surveillance Group in Whom Breast Cancer Developed.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age at Diagnosis</th>
<th>Mutation</th>
<th>Prior Prophylactic Mastectomy</th>
<th>Follow-up after Diagnosis</th>
<th>Current Status*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>4284del5 in BRCA1</td>
<td>No</td>
<td>15</td>
<td>NED</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>IVS12-16del19 in BRCA1 (a 3.8 kb deletion affecting exon 12)</td>
<td>No</td>
<td>41</td>
<td>Died of breast cancer</td>
</tr>
<tr>
<td>3</td>
<td>39</td>
<td>4284del5 in BRCA1</td>
<td>No</td>
<td>18</td>
<td>NED</td>
</tr>
<tr>
<td>4</td>
<td>39</td>
<td>1304del1 in BRCA1</td>
<td>No</td>
<td>31</td>
<td>NED</td>
</tr>
<tr>
<td>5</td>
<td>43</td>
<td>IVS12-16del19 in BRCA1 (a 3.8 kb deletion affecting exon 12)</td>
<td>No</td>
<td>97</td>
<td>NED</td>
</tr>
<tr>
<td>6</td>
<td>44</td>
<td>1154del4A in BRCA1</td>
<td>No</td>
<td>25</td>
<td>NED</td>
</tr>
<tr>
<td>7</td>
<td>49</td>
<td>1068delA + G1665 in BRCA1</td>
<td>Yes</td>
<td>14</td>
<td>NED</td>
</tr>
<tr>
<td>8</td>
<td>53</td>
<td>IVS21-1del5 in BRCA1 (a 4.1 kb deletion affecting exon 22)</td>
<td>Yes</td>
<td>19</td>
<td>NED</td>
</tr>
</tbody>
</table>

* NED denotes no evidence of disease.

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Breast Cancer after Prophylactic Bilateral Mastectomy in Women with a BRCA1 or BRCA2 Mutation

### Table 3. Characteristics of the Tumors in the Eight Women in the Surveillance Group in Whom Breast Cancer Developed.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Tumor Size</th>
<th>No. of Positive Nodes/Total No. of Nodes</th>
<th>Histologic Type</th>
<th>Depth of Invasion</th>
<th>Neoadjuvant Therapy</th>
<th>Breast Ultrasound</th>
<th>Clinical Examination</th>
<th>Mammography</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25, 13</td>
<td>1/15</td>
<td>Ductul III</td>
<td>Negative</td>
<td>3</td>
<td>SC</td>
<td>SC</td>
<td>SC</td>
<td>PB</td>
</tr>
<tr>
<td>2</td>
<td>40, 11</td>
<td>3/13</td>
<td>Ductul III</td>
<td>Negative</td>
<td>12</td>
<td>SC</td>
<td>SC</td>
<td>SC</td>
<td>PB</td>
</tr>
<tr>
<td>3</td>
<td>18, 0/1 sentinel node</td>
<td>Ductul III</td>
<td>Negative</td>
<td>31</td>
<td>NA</td>
<td>SC</td>
<td>SC</td>
<td>SC</td>
<td>ND</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>5/21</td>
<td>Ductul III</td>
<td>Negative</td>
<td>10</td>
<td>SC</td>
<td>SC</td>
<td>SC</td>
<td>SC</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>6/18</td>
<td>Ductul III</td>
<td>Negative</td>
<td>23</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>PB</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>0/10</td>
<td>Ductul III</td>
<td>Negative</td>
<td>31</td>
<td>SC</td>
<td>SC</td>
<td>SC</td>
<td>PB</td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>0/1 sentinel node</td>
<td>Ductul II</td>
<td>Negative</td>
<td>41</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>SC</td>
</tr>
<tr>
<td>8</td>
<td>15</td>
<td>0/1 sentinel node</td>
<td>Ductul III</td>
<td>Positive</td>
<td>21</td>
<td>NA</td>
<td>NA</td>
<td>SC</td>
<td>SC</td>
</tr>
</tbody>
</table>

* BSE denotes breast self-examination, CBE clinical breast examination, MRI magnetic resonance imaging, SC suspicion of cancer, PB high probability of a benign lesion, ND not done, and NA no abnormalities.
Results

Characteristics of the Women

Table 1 lists the general characteristics of the women who chose to undergo prophylactic mastectomy and those who opted for surveillance. Significantly more women in the mastectomy group than in the surveillance group had undergone a premenopausal oophorectomy (44 vs. 24 [58 percent vs. 38 percent], P = 0.03). All gynecologic cancers occurred before the age of 56 years, the two such cases in the mastectomy group were ovarian cancer, stage IC. There were no significant differences between the two groups with respect to age, average duration of follow-up after entry into the study, follow-up after premenopausal oophorectomy, and type of mutation. The 26 distinct mutations — 23 in BRCA1 and 3 in BRCA2 — were distributed in a similar fashion in the two groups. The 139 women were from a total of 70 families; the number of women from each family ranged from 1 to 8.

The mean (±SE) duration of follow-up was 2.9±1.4 years (219 woman-years) in the mastectomy group and 3.0±1.5 years (190 woman-years) in the surveillance group (Table 1). The total number of woman-years of surveillance increased from 190 to 318 when the 128 woman-years of surveillance before prophylactic mastectomy was added.

Incidence of Breast Cancer

After prophylactic mastectomy no case of invasive breast cancer was observed in any of the 76 women during 219 woman-years at risk (Fig. 1). In the surveillance group eight invasive breast cancers were detected during 318 woman-years at risk, for a yearly incidence of 2.5 percent. The ratio of observed cases to expected cases was 1.2 (8 vs. 6.7, 95 percent confidence interval,
Discussion of the Results

0.4 to 3.7; P=0.80). All the affected women were from different families. The actuarial mean five-year incidence of breast cancer in the women in the surveillance group (Fig. 1) was 17 ±7 percent, but the number of women at risk at five years was only eight. To obtain a more stable estimate with longer periods of follow-up, we calculated cumulative incidence probabilities with the use of an exponential model in which the hazard rate was assumed to be constant. According to this model, the yearly incidence of breast cancer was 2.5 percent and the five-year cumulative incidence was 12 percent (95 percent confidence interval, 6 to 23 percent) (Fig. 1). Disregarding the years of surveillance before prophylactic mastectomy and thus restricting the actuarial analysis to the 63 women in the surveillance group, we estimated that the five-year risk of breast cancer was 24.9 percent.

Cox proportional hazards analysis showed that mastectomy significantly (P=0.003) decreased the incidence of breast cancer (hazard ratio, 0.95 percent confidence interval, 0.6 to 0.36). After adjustment for the effect of age and menopausal status, the protective effect of mastectomy remained statistically significant (P=0.01).

Outcome in the Women with Breast Cancer

None of the eight patients in the surveillance group in whom breast cancer developed had been scheduled to undergo prophylactic mastectomy at the time of the diagnosis. The characteristics of the women and the tumors are described in Tables 2 and 3, respectively. Patients 7 and 8 underwent bilateral oophorectomy 14 and 12 months, respectively, before the diagnosis of breast cancer. Of the eight cancers, four (in Patients 1, 2, 4, and 6) were detected between screening sessions (so-called interval cancers). In these four patients the interval from screening to diagnosis was two to five months. The cancers in the other four patients (Patients 3, 5, 7, and 8) were detected during a screening session. Patient 1 became symptomatic eight weeks after her first clinical breast cancer screening, the results of which were negative. In four of the eight patients, breast cancer was detected before the molecular diagnosis was made.

Histologic Findings in the Mastectomy Group

Invasive cancer was not detected in any of the specimens obtained at the time of prophylactic mastectomy. One 44-year-old woman with a BRCA1 mutation had lobular carcinoma in situ.

DISCUSSION

In this prospective study we assessed the incidence of breast cancer in 139 women with a BRCA1 or BRCA2 mutation who chose to undergo either prophylactic mastectomy or regular surveillance. Whereas breast cancer developed in 8 of 63 women in the surveillance group, no cases of breast cancer occurred among the 76 women who underwent prophylactic mastectomy. The observed number of breast cancers in the group under surveillance is compatible with the reported incidence of breast cancer in women with a BRCA1 or BRCA2 mutation. As compared with the incidence in the surveillance group, the incidence of breast cancer in the prophylactic-mastectomy group was significantly reduced (P=0.003), but the mean follow-up of three years calls for a cautious interpretation of our results.

Table 2. Characteristics of the Eight Women in the Surveillance Group in Whom Breast Cancer Developed.

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Age at Diagnosis</th>
<th>Mutation</th>
<th>Risk Oophorectomy</th>
<th>Follow-up after Diagnosis</th>
<th>Current Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24</td>
<td>4298delAG in BRCA1</td>
<td>No</td>
<td>18</td>
<td>NED</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>11V123663C885 in BRCA1</td>
<td>No</td>
<td>41</td>
<td>Died of breast cancer</td>
</tr>
<tr>
<td>3</td>
<td>39</td>
<td>11V123663C885 in BRCA1</td>
<td>No</td>
<td>18</td>
<td>NED</td>
</tr>
<tr>
<td>4</td>
<td>39</td>
<td>2094delGA in BRCA1</td>
<td>No</td>
<td>18</td>
<td>NED</td>
</tr>
<tr>
<td>5</td>
<td>41</td>
<td>11V123663C885 in BRCA1</td>
<td>No</td>
<td>97</td>
<td>NED</td>
</tr>
<tr>
<td>6</td>
<td>41</td>
<td>11V123663C885 in BRCA1</td>
<td>No</td>
<td>97</td>
<td>NED</td>
</tr>
<tr>
<td>7</td>
<td>41</td>
<td>11V123663C885 in BRCA1</td>
<td>No</td>
<td>97</td>
<td>NED</td>
</tr>
<tr>
<td>8</td>
<td>41</td>
<td>11V123663C885 in BRCA1</td>
<td>No</td>
<td>97</td>
<td>NED</td>
</tr>
</tbody>
</table>


tomy, women with a BRCA1 or BRCA2 mutation may choose to undergo bilateral oophorectomy before menopause, chemoprevention, or both to reduce the risk of breast cancer. Such interventions may reduce the risk of breast cancer by about 50 percent, but the use of tamoxifen as a preventive agent has been questioned in view of its long-term side effects.

Prophylactic mastectomy is a highly personal decision. In counseling high-risk women, the protective effect of prophylactic mastectomy must be weighed against possible surgical complications and psychological problems. Up to 30 percent of the women who undergo the procedure will have surgical complications, depending on the type of surgery and the length of follow-up.58 A long-term study of prophylactic mastectomy reported unanticipated repeated operations in 49 percent of women, but these results may not be applicable to prophylactic mastectomies as they are currently performed. Psychological studies of women who had undergone a prophylactic mastectomy did not find that, overall, the procedure had detrimental effects on body image and sexuality.88

In conclusion, our data and those of Hartmann et al.88 indicate that prophylactic bilateral total mastectomy substantially reduces the incidence of breast cancer among women with a BRCA1 or BRCA2 mutation. Nevertheless, longer follow-up and studies of more patients are required to establish the protective effect and determine the long-term complications of this procedure.

Suggested in part by a grant from the Dutch Cancer Society (DIEK 05-195) and a grant from the National Institutes of Health (N01CA126183). The authors thank Dr. Karen Duren for the data collection, to Didi Halley and Peter Denzler for manuscript editing, and to Petra Reit for assistance with the preparation of the manuscript.

REFERENCES

Path of Publications

Primary Resources → Secondary Resources → Tertiary Resources
Types of Research Information
Secondary Sources

• **Definition**- interpret and analyze primary sources. They are a step removed from the event or original product.

• **Examples**
  - Textbooks
  - Magazine or newspaper articles
  - Criticisms & commentaries
  - Systematic reviews, meta analyses/syntheses
  - Web sites
Examples of Secondary Sources

REVIEW
A systematic review of advanced practice nurses’ skin cancer assessment barriers, skin lesion recognition skills, and skin cancer training activities

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2 Medical Directors, Inc., Tucson, Arizona
3 The Skin Cancer Institute, Phoenix Cancer Center, The University of Arizona, Tucson, Arizona

Abstract
Purpose: Limited is known about the skin cancer detection skills of advanced practice nurses (APNs). This systematic review of published literature seeks to describe any barriers to APNs’ performance of skin examinations, if APNs’ ability to recognize suspicious skin lesions, and if APNs’ skin cancer detection training activities.

Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the quality of reporting standards were used to conduct a comprehensive search of CINAHL, PubMed, Web of Science, and Ovid databases and interpretation of findings. Of the 315 articles and abstracts identified for selection, 121 were selected for full review.

Conclusions: Barriers to skin examination by APNs have been inconsistently measured. Limited time to conduct skin examinations is the most consistent barrier. APNs’ ability to recognize and refer suspicious and benign lesions is inconsistent, but shows improvement after training. Few skin cancer detection resources are available for APNs.

Hospital Compare

Hospital Compare is a consumer-oriented website that provides information on how well hospitals provide recommended care to their patients. This information can help consumers make informed decisions about health care. Hospital Compare allows consumers to select multiple hospitals and directly compare performance measures related to heart attack, heart failure, pneumonia, surgery, and other conditions. These results are organized by:

- Hospital Survey Results
- Timely and Effective Care
- Readmissions, Complications, and Deaths
- Use of Medical Imaging
- Linking Quality to Payment
- Medicare Volume

Access the Hospital Compare Web site at www.hospitalcompare.hhs.gov

Hospital Compare was created through the efforts of Medicare and the Hospital Quality Alliance. The Hospital Quality Alliance (HQA) was formed in December 2002. The HQA was a program collaboration established in December 2002 to promote reporting on hospital quality of care. HQA consisted of organizations that represented consumers, hospitals, doctors, employees, accrediting organizations, and federal agencies. The HQA effort was intended to make it easier for consumers to make informed health care decisions and to support efforts to improve quality in U.S. hospitals. Since its inception, many new measures and topics have been displayed in the site.
**Types of Research Information**

**Tertiary Sources**

- **Definition**
  - indexes, compiles or organizes citations to secondary and primary sources
  - Takes information from secondary sources and condenses or reformats it into an easy-to-read form

- **Examples**
  - Databases such as CINAHL, PubMed
  - Almanacs & guidebooks
  - Textbooks
  - Encyclopedias
  - Manuals and handbooks
  - Dictionaries
Examples of Tertiary Sources
Aging and Attentional Bias for Death related and General Threat-related Information: Less Avoidance in Older as Compared With Middle-Aged Adults

Redi De Raedt, Ernst H. W. Koster, and Ruben Ryckewaert

Department of Experimental Clinical and Health Psychology, Ghent University, Belgium.

Objective. The aging literature suggests that life satisfaction and affective well-being stabilizes or even increases during the aging process, and that death anxiety would decrease with aging. Experimental psychology literature shows that emotional-potential role in information processing. The aim of the current study was to investigate whether death-related and neutral threat words would lead to less and less attentional processing in middle-aged versus older adults.

Method. Twenty-seven older adults between 74 and 90 years and 31 middle-aged adults between 40 and 50 years participated in the study. We used questionnaires to assess death anxiety and an emotional attentional task to measure attention toward death-related versus general threat words.

Results. Our results showed no age-related differences in self-reported death anxiety, but less attentional avoidance of threat in older adults. We failed to demonstrate differences between general and death-related threat.

Discussion. This is the first study investigating attentional processing of both death- and threat-related information in older versus young adults. Less avoidance toward threat suggests that with aging, death becomes less of a concern, which might be indicative of acceptance of the own imminent old age.

Key Words: Aging—Attentional bias—Death anxiety—Threat.
Observation bias in randomized clinical trials with measurement scale outcomes: a systematic review of trials with both blinded and nonblinded assessors

Abstract

Background: Clinical trials are commonly done without blinded outcome assessors despite the risk of bias. We wanted to evaluate the effect of non-blinded outcome assessment on pooled differences in effect size using inverse variance random-effects meta-analysis and used metaregression to identify potential reasons for variation.

Competing interests: Frida Emanuelsson and Ann Sofla Skou Thomsen have received grants from the Danish Council of Research.
Quiz Answers

• Picture A – Secondary
• Picture B - Primary
• Picture C - Tertiary
• Picture D – Secondary
• Picture E – Secondary
• Picture F – Primary